

1. (Thrice Amended) A system for determining experimentally a plurality of three-dimensional atomic structures, each of which is associated with a corresponding protein, comprising:

a database of sequence information for a plurality of proteins, and structural information and functional information for selected proteins;

at least one bioinformatics tool adapted to use the sequence information, structural information and functional information stored in the database to cluster the plurality of proteins into a plurality of families, in which, for each family, members of the family have corresponding homologous sequences;

protein synthesis means for synthesizing for each family determined by the at least one bioinformatics tool a plurality of target proteins which are members of the family, using information stored in the database corresponding to the target proteins, the protein synthesis means having screening means for screening products of the synthesis to choose selected synthesized products for processing;

protein processing means for preparing, purifying and characterizing each of the selected synthesized products;

crystallization means for crystallizing the processed synthesized product against a plurality of crystallization screens to produce a plurality of specimen crystals of the target protein, and testing the plurality of specimen crystals for predetermined diffraction characteristics to determine suitable specimen crystals;

X-ray crystallography means for performing high-throughput crystallography on the specimen crystals of each target protein determined by the crystallization means to be suitable, the X-ray crystallography means having diffraction measuring means for

measuring for diffraction data the suitable specimen crystals of the target protein, analyzing means for analyzing the diffraction data, means for building an atomic model of the target protein according to an analysis of the diffraction data by the analyzing means, and means for refining the model of the target protein against the diffraction data and storing the refined model in the database;

structure extraction means having means for analyzing the refined model of the target protein using sequence information corresponding to other family members which is stored in the database and structural information corresponding to other proteins which is stored in the database, means for analyzing the refined model for functional motifs and for surface characteristics to define active sites and macromolecular contact sites, and means for defining at least one class of compounds predicted to have binding potency using the active sites information corresponding to the target protein; and

a homology model building tool adapted to use the refined model of the target protein retrieved from the database to develop a homology model of one or more predicted protein structures,

wherein the database is updated using the at least one bioinformatics tool and the developed homology model.

2. (Twice Amended) A system according to claim 1, further comprising:

cryoprotection means for freezing the suitable specimen crystals,

wherein the suitable specimen crystals are frozen by the cryoprotection means before being measured for diffraction data

by the diffraction measuring means.

6. (Twice Amended) A system according to claim 1, wherein the homology model developed by the homology model building tool is used in at least one of target selection, drug design, and design of constructs for experimental analysis.

7. (Thrice Amended) A process for determining experimentally a plurality of three-dimensional atomic structures, each of which is associated with a corresponding protein, comprising the steps of:

(a) systematically organizing sequence information for a plurality of proteins, and structural information and functional information for selected proteins into a database;

(b) clustering the plurality of proteins into a plurality of families, in which, for each family, members of the family have corresponding homologous sequences, using at least one bioinformatics tool and the sequence information, structural information and functional information stored in the database;

(c) synthesizing for each family determined in step (b) a plurality of target proteins which are members of the family, using information stored in the database corresponding to the plurality of target proteins, and screening products of the synthesis to choose selected synthesized products for processing;

(d) preparing, purifying and characterizing each synthesized product that is chosen in step (c);

(e) crystallizing the processed synthesized product prepared, purified and characterized in step (d) against a plurality of crystallization screens to produce a plurality of specimen crystals of the target protein;

(f) testing the plurality of specimen crystals grown in step (e) for predetermined diffraction characteristics to determine suitable specimen crystals of the target protein;

(g) performing high-throughput crystallography, including measuring for diffraction data the specimen crystals determined in step (f) to be suitable, building an atomic model of the target protein according to an analysis of the diffraction data, refining the model of the target protein against the diffraction data, and storing the refined model in the database;

(h) analyzing the refined model, stored in the database in step (g), of the target protein using sequence information corresponding to other family members which is stored in the database and structural information corresponding to other proteins which is stored in the database, analyzing the refined model of the target protein for functional motifs and for surface characteristics to define active sites and macromolecular contact sites, and defining at least one class of compounds predicted to have binding potency using the active sites information corresponding to the target protein;

(i) developing a homology model of one or more predicted protein structures using computational tools for homology model building and the refined model of the target protein retrieved from the database, and updating the database by using the at least one bioinformatics tool and the developed homology model; and

(j) performing steps (f) through (i) for each of the other target proteins.

8. (Twice Amended) A process according to claim 7, further comprising the step of:

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Page B-5

freezing the specimen crystals of the target protein which are determined in step (f) to be suitable,

wherein the suitable specimen crystals are frozen before being measured for the diffraction data in step (g).

12. (Twice Amended) A process according to claim 7, further comprising the step of

using the homology model developed in step (i) in at least one of target selection, drug design, and design of constructs for experimental analysis.